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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/764,141

01/19/2001

Peter N. Devreotes

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06/07/2004

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EXAMINER

CHANDRA, GYAN

ART UNIT

PAPER NUMBER

1646

DATE MAILED: 06/07/2004

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/764,141

Applicant(s)

DEVREOTES ET AL.

Examiner

Gyan Chandra

Art Unit

1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 March 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-76 is/are pending in the application.
- 4a) Of the above claim(s) 1-10, 26-55 and 58-76 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11-25, 56 and 57 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-76 are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03 July 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 5/27/04.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Applicant's election of 11-25 and 56-57 in Paper No.11 March 2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-10, 26-55 and 58-76 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse based on an incomplete response.

Claim Objections

Claims 11 and 56 are objected to because of the following informalities: The claims specifically recite nonelected subject matter i.e., γ subunit of G protein. Appropriate correction is required.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested " Heterotrimeric G-protein"

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-25, 56, 57 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a functional heterotrimeric G protein comprising an α subunit comprising a first amino acid sequence encoding a first fluorescent protein and a β subunit comprising a second amino acid sequence encoding a second fluorescent protein, wherein said first and second fluorescent proteins are capable of fluorescence resonance energy transfer (FRET), does not reasonably provide enablement for a functional heterotrimeric G protein comprising an α subunit comprising a first amino acid sequence encoding a first luminescent protein and a β subunit comprising a second amino acid sequence encoding a second luminescent protein, wherein said first and second luminescent proteins are capable of bioluminescence resonance energy transfer (BRET). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed to α subunit and β subunit of a functional heterotrimeric G-protein. The specification teaches in general about inserting cyan fluorescent protein (CFP) into a Spe I site after the residue 90 between the α A and α B helices of the Ga2 cDNA of Dictyostelium discoideum (References and Notes 12). Inventors briefly mentioned about placing the Yellow fluorescent protein to the N-terminus to β subunit of G-heterotrimer protein and this could be a guide for a skilled person to take a next step.

Biondi et.al. (1988) teach the method and use of green fluorescent protein (GFP) fusion with two different protein subunits to obtain information on regions essential for protein function. They performed the random insertion of GFP into the cAMP-dependent protein kinase regulatory subunit from *D. discoideum*. Inventors performed fusion of cyan and yellow fluorescent coding sequence with the α or β subunits of G-protein. Inventors accept the idea that the insertion of CFP in the α subunit can be done at different amino acid positions. However, the inventors pointed out that the distance between the acceptor and donor fluorescent moieties should be less than 100 angstroms.

A large number of experimentation would be required to make luminescent G-protein fusions that would be capable of BRET because specification does not provide any details on which luminescent protein to use and how to attach a luminescent protein with α or β subunits of G-protein.

The amount of guidance or direction provided by specification with regard to luminescent G-protein subunits capable of BRET is very small and would require a large amount of experimentation as Pflieger et.al. (2003) report that the BRET signal is dependent upon the spectral properties, ratio, distance and relative orientation of the donor and acceptor molecules, as well as the strength and stability of the interaction between proteins of interest.

There are no working examples directed to BRET so that one can easily translate FRET into BRET without undue experimentations. Angers et.al. (2000)

applied the BRET technology in detecting β 2-adrenergic receptor dimerization in living cells.

The state of the art with regard to BRET is evolving. A number of reports have recently been published for the use of this technology in studying protein – protein interactions (Angers et.al., 2002; Jensen et.al., 2002; Zeng et.al., 2003).

The BRET system is complex because it requires a person skilled in the field to identify which luminescent protein one needs to attach with the α subunit and which luminescent protein with the β subunit of G-protein.

It is unpredictable which luminescent G-protein subunits would be capable of BRET because bioluminescence would require an optimization of distance between the donor and acceptor bioluminescent subunits of G-protein.

The claims are very broad, in that the claims do not specify where the luminescent proteins should be attached to what positions of the α and β subunits of G-protein.

Due to the large quantity of experimentation necessary to determine a luminescent G-protein fusion such that it can be determined how to use the claimed BRET, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art establishing that the BRET assay can not be predicted based on FRET information, and the breadth of the claims which fail to recite particular luminescent protein, the specification fails to teach the skilled artisan how to make and use the claimed invention.

Conclusion

No claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

1. Biondi et.al., Nucl. Acids Res. 26:4946-52 (1988).
2. Jensen et.al., Eur. J. Biochem. 269:5076-87 (2002).
3. Zeng et.al., Mol. Pharmacol. 64: 1474-84 (2003).
4. Pflieger et.al., Pituitary 6:141-51 (2003).
5. Angers et.al., Proc. Nat. Acad. Sci. 97: 3684-89 (2000).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gyan Chandra whose telephone number is (571)272-2922. The examiner can normally be reached on 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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1June 2004



ELIZABETH KEMMERER
PRIMARY EXAMINER